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Outbreak Investigation by "Disease Detectives": A Retrospective Analysis of Hospital Infection Control Practices

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ABSTRACT

Introduction: Outbreaks in the intensive care units have a devastating impact in any healthcare setting, especially Tertiary care hospitals. Conventionally, outbreaks have been described using the "shoe leather" approach. Understanding of emerging infectious microorganisms requires laboratory isolation as a vital tool in investigation of outbreaks. Notorious microorganisms are commonly associated with such outbreaks. This requires "disease detectives" to maintain a constant vigil.

Material & methods: In this analytical study we summarize five outbreaks at our Tertiary care centre over a period of 18 months. The outbreaks were investigated by the Infection control team following the recommendations of CDC (10 step approach).

Results & Discussion: Three outbreaks occurred in the adult intensive care unit (ICU). Gram negative organisms (Acinetobacter spp & Chryseobacteriumindologenes) predominated as etiological agents(66%) from blood, urine and endotracheal tube aspirates. All outbreaks in the Neonatal ICUs were caused by Acinetobacter spp., which was isolated from blood samples of neonates. Despite our vigorous efforts the source was identified only in one outbreak. Significant mortality was seen in all outbreaks (probably multifactorial).

Conclusion: A constant scrutiny especially in the high risk areas can help in limiting the number of cases and timely intervention cannot let the micro-organisms escape unfathomed.

Key Words: *Outbreak, infection control, nosocomial infection, investigation, multidrug resistant organisms*

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INTRODUCTION:

Outbreaks in the healthcare setting have a huge impact on patient care and safety, both in public and private settings. Healthcare setups, apart from providing diagnostic and therapeutic facilities to population at large, also condition microorganisms. Micro-ecosystems exist in healthcare settings, particularly in high-risk areas like ICU, Dialysis units, endoscopy rooms. Notorious microorganisms may exist as complex communities in the form of biofilms making routine disinfection and cleaning practices ineffective. An outbreak may result due to a mosaic of environment, host and microorganism related factors.

Outbreak has been defined as an occurrence of more cases of disease than expected in a given area among a specific group of people over a particular period of time[1]. The term pseudo-outbreak has also been referred to in literature, being defined as an increase in identified organisms but without evidence of infection[2]. Outbreaks have been reported time and again throughout the world, however this may just represent the tip of an iceberg[3]. Even when outbreaks are reported, they are not investigated systematically.In most cases there is a lack of guidelines and policies at the institutional level for healthcare associated infection (HAI) outbreak detection and response, especially in low and middle income countries. Now if we question the need to investigate an incline in number of cases and expose our current infection control measures, the answer is still an affirmative one. There is definitely a need, to identify the etiological agent, take appropriate measures for controlling outbreak, assess existing policies in an institution and make necessary changes to prevent future outbreaks; for research and epidemiological purposes and to minimize financial implications borne by the healthcare system as a whole[3].

The CDC describes a classic "10 step" approach for the systematic investigation of an outbreak. (Table 1) Conventionally "shoe leather" approach has been utilized to describe outbreaks[2]. The role of the Microbiology laboratory is central in investigating and defining an outbreak in modern times, more so for emerging infectious diseases, especially seen during the Covid 19 pandemic. Microbiologists along with other members of the infection control team of a hospital act as "disease detectives" to maintain a constant vigil for tracking and containing outbreaks. We conducted this analytical study to reinforce that in resource limited settings, a basic setup with a Microbiology laboratory andan active infection control team can detect these "outbreaks" at the earliest and prevent devastating impacts on healthcare. Preventing outbreaks of infectious diseases can be made possible by continuous ongoing active prospective surveillance by an alert infection control team.

Table 1: CDC approach to investigate an outbreak

STEP	DESCRIPTION
1	PREPARE FOR FIELD WORK
2	CONFIRM THE DIAGNOSIS
3	DETERMINE THE EXISTENCE OF AN OUTBREAK
4	CREATE A CASE DEFINITION AND PREPARE LINE-LIST OF CASES
5	TABULATE DATA IN TERMS OF TIME, PLACE AND PERSON (DESCRIPTIVE EPIDEMIOLOGY)
6	CONSIDER IMPLEMENTATION OF CONTROL MEASURES
7	DEVELOP AND TEST HYPOTHESIS
8	PLAN FOR SYSTEMATIC STUDIES
9	IMPLEMENT CONTROL AND PREVENTIVE MEASURES
10	COMMUNICATE FINDINGS

METHODOLOGY:

This retrospective analytical study was conducted in a 500 bedded tertiary care hospital of North Delhi over a period of 18 months in the department of Microbiology. The department is an integral part of Infection Control team along with four infection control nurses. One of the most important tasks that the dedicated Infection Control team performs is tracking of infectious disease outbreaks both actively and passively.Surveillance is done regularly at the Microbiology laboratory level. Suspected cases of HAI are noted and followed upon a daily basis.Clustering of cases from a single source indicates a probable outbreak and it is further worked up.An outbreak was defined as two or more cases of a particular type of HAI due to the same offending microorganism, occurringin a given place in a specified period of time (higher occurrence than expected for our hospital).A total of five outbreaks were identified over a period of 18 months, between October 2017 and March 2019.These outbreaks were investigated by the Infection control team following the recommendations of CDC (10 step approach).Source tracking was also attempted through cultures of environmental samples.Standard protocol was used to identify the microorganisms and antibiotic susceptibility pattern was recorded following the CLSI guidelines.Identification and susceptibility profiles ofthe matching isolates was confirmed with Automated ID/AST system (Microscan).

Result

Three outbreaks occurred in the adult ICU, two of which were caused by Gram negative organisms (*Acinetobacter baumanii*&*Chryseobacteriumindologenes*) & one by gram positive organism (Glycopeptide resistant *Enterococcus faecium*). These were isolated from blood, urine and endotracheal tube aspirate specimens respectively. *Acinetobacter baumanii* was identified to be the cause of other two outbreaks that were reported from neonatal ICUs. These were from blood samples.

Table 2 summarizes all the 5 outbreaks, individual outbreaks are described in table 3.

Table 2: Summary of all outbreaks between October 2017 and March 2019

	Outbreak1	Outbreak 2	Outbreak 3	Outbreak 4	Outbreak 5
Location	Inborn nursey	General ICU	NICU	General ICU	General ICU
Event time frame	Nov 2017 (8 days)	December 2017 (1 month)	July 2018 (7 days)	August 2018 (1 day)	Nov 2018- March 2019 (4 months)
No. of cases	5	5	5	4	7

Etiological agent	*Acinetobacter baumanii*	*Glycopeptide resistant Enterococcus faecium*	*Acinetobacter baumanii*	*Acinetobacter baumanii*	*Chryseobacteriumindologenes*
Source of organism	Blood	3 isolates-blood 2 isolates-urine	Blood	Blood	1 isolate-blood 6 isolates-Endotracheal aspirate
Environmental source identification	No (Central oxygen point, different species-*Acinetobacter lwofii* isolated)	No	Yes (weighing machine)	No	No
Similar antibiogram of patient and environmental isolate	No	--	Yes (Sensitive to Polymyxin B, tigecycline and resistant to piperacillin-tazobactam, amikacin, meropenem, ceftazidime, Cefoperazone-sulbactam)	--	--
Outcome in terms of mortality*	4	3	2	2	4

*Since all these patients were sick and admitted with other life threatening conditions, direct causal relationship with infectious agents could not be established.

Table 3: Description of individual outbreaks between October 2017 and March 2019

Outbreak	Organism	Case no. and Sample	Date of receiving sample	Diagnosis	Risk.factor/co-morbidity	Outcome
1 (Inborn nursery)	*Acinetobacter baumanii*	1 (Blood)	2/11/2017 (Day 1)	Hyaline membrane disease, Respiratory distress, Respiratory failure	Preterm and Very low birth weight	Expired
		2 (Blood)	3/11/2017 (Day 2)	Gastrointestinal (GI) bleed with meconium stained liquor	--	Expired
		3 (Blood)	3/11/2017 (Day 2)	Respiratory failure	Pneumonia	Expired
		4 (Blood)	7/11/17 (Day 6)	Hypoglycemia with metabolic disorder	--	Recovered
		5 (Blood)	9/11/17 (Day 8)	Hyaline membrane disease with shock	Pre term and Low birth weight	Expired
2 (ICU)	Glycopeptide resistant Enterococcus	1 (Blood)	1/12/2017 (Day 1)	Acute exacerbation of Chronic obstructive pulmonary disease (COPD)	Hypertension	Expired
		2 (Urine)	7/12/2017 (Day 7)	G3P2L1 with Thrombotic microangiopathy with Lower respiratory tract infection (LRTI)	--	Recovered
		3	11/12/2017	Respiratory distress	--	Expired

		(Urine)	(Day 11)			
		4 (Blood)	15/12/2017 (Day 15)	Coronary artery disease with LRTI, Pancytopenia	Hypertension, Age>80 years	Expired
		5 (Blood)	22/1/2017 (Day 22)	COPD with respiratory failure	Diabetes mellitus, Hypertension, Age: 60 years	Recovered
3 (NICU)	*Acinetobacter baumannii*	1 (Blood)	06/07/2018 (Day 1)	Severe anaemia with septic shock	--	Expired
		2 (Blood)	18/07/2018 (Day 13)	Septic shock	Pre-term	Recovered
		3 (Blood)	18/07/2018 (Day 13)	Respiratory failure with shock	Pre-term, mechanical ventilation	Recovered
		4 (Blood)	20/07/2018 (Day 15)	GI bleed with sepsis	Pre-term, Very low birth weight	Expired
		5 (Blood)	23/07/2018 (Day 18)	Respiratory failure	--	Recovered
4(ICU)	*Acinetobacter baumanii*	1 (Blood)	6/8/2018 (Day 1)	Renal failure with septicemia	--	Expired
		2 (Blood)	6/8/2018 (Day 1)	Cerebrovascular accident (CVA)	Diabetes mellitus type 2	Expired
		3 (Blood)	6/8/2018 (Day 1)	Placenta previa	--	Recovered
		4 (Blood)	6/8/2018 (Day 1)	Hypothyroidism	Diabetes mellitus type 2 with hypertension	Recovered
5 (ICU)	*Chryseobacteriumindologenes*	1 (ETA)	12/11/2018 (Day 1)	CVA	Diabetes mellitus, hypertension, bed sore, age>70	Expired
		2 (ETA)	22/11/2018 & 6/12/2018 (Day 11, 25)	Acute respiratory distress syndrome with swine flu	--	Expired
		3 (Blood)	14/12/2018 (Day 30)	Pulmonary tuberculosis	--	Expired
		4 (ETA)	20/12/2018 (Day 37)	Organophosphorous poisoning	--	Recovered
		5 (ETA)	11/2/19 (Day 59)	Pneumonitis with restricted lung disease	Age: 12 years	Recovered
		6 (ETA)	11/3/2019 (Day 87)	Hanging, hypoxic encephalopathy	--	Recovered
		7 (ETA)	11/3/2019 (Day 87)	LRTI with CVA	COPD, Age> 70 yrs	Expired

Outbreak 1

The first outbreak was recorded in the inborn nursery in November 2017. *Acinetobacter baumanii* was isolated from blood samples of five newborns over a span of 8 days. Two of these had respiratory failure who along with two

othersexpired. Recovery rate in this outbreak was 20%. Environmental sampling was done from suction machine, beds, humidifiers & central oxygen point. *Acinetobacter spp.*wasisolated from the central oxygen point. However, the biotypingand antibiograms did not match. The findings were communicated to the unit head andnursing in-charge.Strict disinfection & isolation precautions were recommended by the infection control team. Repeat environmental samples taken after a week did not show any growth.

Outbreak 2:

The second outbreak includedfive isolates of Glycopeptide resistant *Enterococcus*, from general/medicine ICU in December 2017.Three of theseisolates were from blood samples and two from urine samples.Glycopeptide resistance was confirmed using panels from Microscan and using epsilometer strips as well. Environmental sampling was done from patients' immediate surroundings, including high touch surfaces. No organism was isolated on repeated attempts of trying to find a source of the offending organism.Strict disinfection & isolation precautions were recommended, and the outbreak was controlled.Recovery rate was 40%.

Outbreak 3

*Acinetobacter baumanii*caused an outbreak in July 2018 in NICU of our tertiary care hospital.These isolates were recovered from blood specimens of five neonates in a time interval of 7 days. The recovery rate in this outbreak was 60%. Environmental sampling was done from weighing machine, suction machine, baby cot, ventilator circuit, humidifier and CPAP machine.*Acinetobacter baumanii*was isolated from the baby weighing machine. On biotyping it was found that the isolate was similar to isolates causing the outbreak. All six isolates (five clinical and one environmental), showed similar antibiotic susceptibility. They all were susceptible to polymyxin B and tigecycline but resistant to piperacillin-tazobactam, amikacin, meropenem, ceftazidime and cefaperazone-sulbactam. Strict disinfection & isolation precautions wererecommendedto the NICU staff and the outbreak was controlled.

Outbreak 4

Acinetobacter baumanii was responsible for the fourth outbreak that was recorded during our study period. This outbreak was different from the remaining four because it was a point source outbreak in medical ICU. Simultaneously four isolates of the aforementioned organism were identified from blood specimens of four different patients.Swabs for environmental sampling were taken from the patients' immediate surroundings including high touch surfaces:handrails of beds, side stools, instruments. No organism was isolated on repeated attempts of trying to find a source of the offending organism.Strict disinfection & isolation precautions were recommended and the outbreak was controlled. The recovery rate in this outbreak was 50%.

Outbreak 5

The fifth outbreak involved seven isolates of *Chryseobacteriumindologenes*over a time interval of 4 months (November 2018 to March 2019). One to two isolates of the organism were recovered each month. Six isolates were identified from endotracheal aspirate specimens and one from blood from General ICUpatient.The characteristic orange yellow pigment and inability of *Chryseobacteriumindologenes*to grow on MacConkey agar were key identifying features which led to a constant vigil in the ICU. Repeated sampling was done in all patients to confirm the diagnosis. No organism was isolated on repeated attempts of trying to find a source of the offending organism.Strict disinfection & isolation precautions were recommended every time, still the outbreak lasted four months.Forty three percent patients recovered (3/7).

The outbreaks are graphically represented in Figure 1

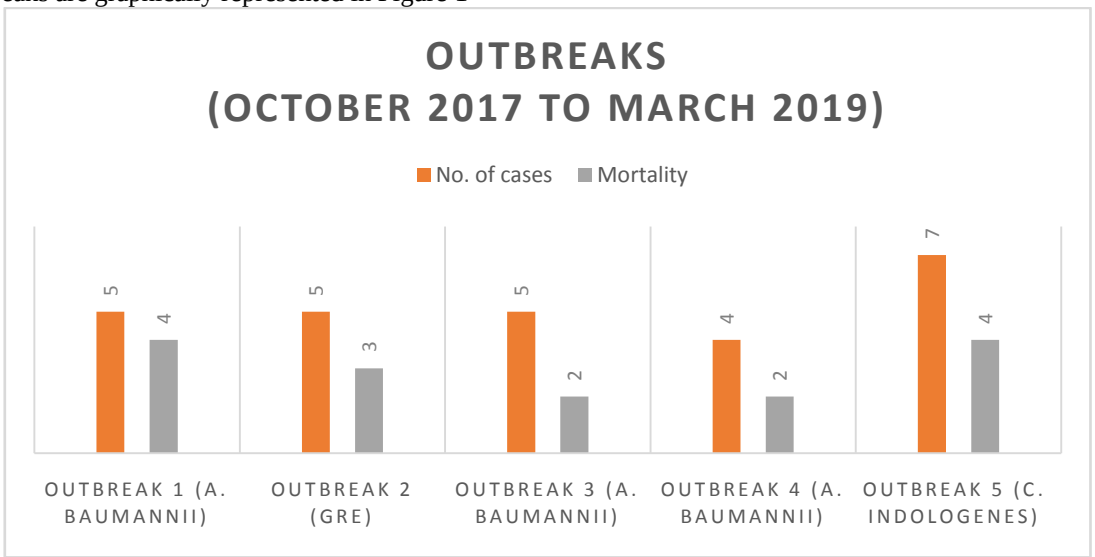

Figure 1: Graphical representation of the outbreaks between October 2017 and March 2019

DISCUSSION:

Majority of intensive care unit infections are caused by Multidrug resistant and Extensively drug resistant organisms, especially the ESKAPE group. This group includes *Enterococcus faecium*, Methicillin resistant *Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, Enterobacter* spp[4]. Outbreaks which were recorded in our study period were caused by *Acinetobacter baumannii*(3), Glycopeptide resistant *Enterococcus*(1) and *Chryseobacteriumindologenes*(1). All three bacteria are commonly seen in the setting of outbreaks in healthcare facilities[5,6,7].

*Acinetobacter baumanii*belongs to genus *Acinetobacter* and members of this genus are gram negative cocco-bacilli. They areare known to survive in health care settings for long periods of time[8]. It is also found in water, soil, 40% healthy individuals[8]. It can contaminate gowns, gloves and can be transmitted by the airborne route[9,10]. They are also known to acquire resistance genes quickly, probably explaining the important role it plays in nosocomial infections[11]. A systematic review published in 2018 by Wieland et al reveals 150 outbreaks were seen between 2000 and 2015 that were caused by *Acinetobacter baumanii.* Majority of these were reported from ICUs with history of prolonged use of antimicrobials and during mechanical ventilation[12]. *Acinetobacterbaumanii*caused both outbreaks that occurred in the our NICU. Interestingly all 3 outbreaks caused by this organism in our study were blood stream infections. There are various reports of nosocomial bacteremia being caused by this organism[13,14]. A review of the outbreaks caused by *Acinetobacter baumanii*between 1977 and 2000 highlights that 56% of the outbreakscaused in this period were respiratory infections and the common source wherever detected, was contaminated respiratory equipment, humidifiers and patient bedding[15]. Source of *A. baumannii* infections could be traced to NICU weighing machine in one of the outbreaks, though in other two outbreaks, source could not be found. The strains isolated from all three outbreaks had a similar sensitivity profile, being susceptible to only colistin and tigecycline. These are last resort antibiotics highlighting the burden of multidrug and extensively drug resistant organisms (MDROs and XDROs) in ICU settings. Also, there could be the same strain of *A. baumannii* circulating among different ICUs in the same hospital. Mortality rates in these outbreaks were 80%, 40% and 50% respectively. Mortality rate in the first outbreak is much higher compared to those reported for outbreaks between 2000 and 2018(around 47%)[12].

Enterococci are known to colonize the gastrointestinal tract for months to years[16, 17]. ICU stays is one of the important risk factor for colonization as there is exposure to antimicrobials[18]. Three isolates during the GRE outbreak were from blood and two from urine specimens. The mortality rate was 40% overall; 67% among bacteremia cases. Previous studies have shown the mortality rates for bacteremia to vary between 17-100%[19]. Despite repeated attempts of environmental sampling, the source of this outbreak could not be identified. Studiesin the past have shown that the hands of healthcare workers are the most consistent source of transmission[20]. An individual acquires vancomycin resistant enterococcus through person to person contact or being exposed to contaminated surfaces. When an individual undergoes prolonged antimicrobial therapy, VRE that had colonized the gut flourishes and may manifest as disease duringimmune suppressed states[21].This outbreak was successfully controlled in a month by strict vigil on disinfection and cleaning practices being followed in the ICU.

*Chryseobacteriumindologenes*is a gram negative bacilli which is non fermentative in nature.Its incidence is increasing post indiscriminate use of colistin and tigecycline in the healthcare settings[7]. This organism caused the longest outbreak in our study (four months). It cannot however be said if this was a single outbreak with interspersed areas of organism inactivity or different outbreaks by same organism during the said time frame.*C indologenes* caused six cases of ventilator associated pneumonia(86%) and one episode of bacteremia(14%). This is consistent with published reports in literature which document that most cases of *Chryseobacteriumindologenes*infections are nosocomial pneumonia and catheter related bacteremias[22,23,24]. It has been speculated that biofilm formation and intrinsic protease activity are key factors in pathogenesis of nosocomial infections[25]. Literature reviews on *Chryseobacteriumindologenes*bring to light that it is ubiquitous in nature and has a tendency to be recovered from water sources in hospitals and it resists chlorination[7]. It is intrinsically resistant to cephalosporins and carbapenems[26]. Probably this was the reason it could not be isolated from environmental surfaces despite repeated attempts during extended period of this outbreak. An analysis of 215 cases of *Chryseobacteriumindologenes*infections from Taiwan has highlighted the reliable role of cotrimoxazole and cefaperazone-sulbactam in treatment[7]. This study also found out that maybe the role of antibiotics in pneumonia patients is uncalled for as all patients succumbed in their study probably indicating colonization of the respiratory tract by the bacteria. This is contrary to our findings where 50% patients of VAP recovered after appropriate antibiotics were administered.

The outbreaks have been described with respect to timelines in graphical representation. A single point source outbreak was seen in *Acinetobacter baumanii*outbreak caused in the general ICU. Intermittent source outbreak was seen in outbreak 1,2,3 and 5. Describing an outbreak in graphical form can help provide information regarding magnitude, time trend, incubation period and pattern of spread. All these can be valuable inputs for control measures[3]. Ours is a 500 bedded tertiary care teaching hospital and with the optimal utilization of all manpower and technical resources we tried our level best to investigate and control these outbreaks. However, despite an effective infection control protocol and highly dedicated infection control team we cite the following reasons for these outbreaks:

1. Common ICU for Medicine, Surgery and Gynaecology

2. Floating population of Resident doctors
3. Patient related risk factors
4. Breach in compliance to care bundles in ICU
5. Breach in compliance to infection control practices
6. Irregular supply of disinfectants
7. Frequent renovations undertaken in hospital
8. Low nursing staff to patient [ratio] (requirement of critical care nursing personnel)
9. Addition of new equipment without additional staff
10. Infrequent refresher trainings in infection prevention and control

Outbreak control in middle or low income countries is a challenging task with limitations of financial, technical and manpower resources. However, some simple and inexpensive measures can help in timely control, thereby reducing morbidity, mortality and healthcare cost. These include hand hygiene, environmental surface cleaning and disinfection, use of appropriate personal protective equipment and following an antimicrobial stewardship program[27].

Observing five outbreaks in 18 months was an eye-opener for the hospital infection control team. We decided to reinforce the existing infection control practices of the hospital and implement a few changes. A very active role was played by the infection control nurses in training the healthcare workers on various aspects of infection control. Weekly refresher trainings were conducted for healthcare workers. The trainings included hand hygiene, PPE donning and doffing, infection control and biomedical waste management. The most important amongst these was hand hygiene. Hand hygiene is the simplest and most effective tool for preventing HAIs. Trainings were conducted to teach the moments and methods of hand hygiene as per CDC protocol. It was observed that there was an improvement in the hand hygiene compliance rate with time (53.96% in 2017 and 57.34% in 2019). Surveillance of critical areas including ICUs, OTs, pre-operative and post-operative areas was done at a regular interval. Strict disinfection practices were followed in case of unsatisfactory results. Also, a robust antimicrobial stewardship program was started with active participation and communication between clinical departments and department of Microbiology. Quarterly meetings were done to assess the achievements and pitfalls.

LIMITATIONSOF THE STUDY:

Environmental sampling identified the source in outbreak 3only(weighing machine in ICU). We could not identify the source in remaining outbreaks.The surface area of swab is very small in comparison to the environment and to identify the best spot for specimen collection becomes a tedious task. Probably more sites in the infected area and repeated samples may be included next time. Neutralization of disinfectant is also important so that the effect of disinfectant does not linger on when not required. Continuous presence of disinfectant in an area makes the exposed organisms stubborn to their action and maybe even dependent on the disinfectant sometimes, with an added survival advantage. Hence disinfectants should be diluted or neutralized before disposal. Other pitfalls in this study were that we could not attempt molecular characterization of the isolates due to lack of technical support. Also, we could not collect samples from the patients to look out for colonization of the offending bacteria. However, the ultimate goal is to effectively control the outbreak timely, which we were able to achieve.

CONCLUSION

Infection control personnel or ‘disease detectives’ play a major role. A constant scrutiny by a dedicated infection control team helps to limit the outbreak and timely intervention cannot let the micro-organisms spread unfathomed. When it comes to infection prevention and control in hospital, the whole faculty should behave as a team, focus on training all staff and improve healthcare safety. All outbreaks must be immediately notified and reported to concerned authorities without fear of reprisal. Such infection control champions should be encouraged, motivated and appreciated by hospital authorities. Only then a culture of safety can evolve.

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